PRIMARY SPLENOMEGALY OF THE GAUCHER TYPE.

A REPORT ON THE SECOND OF FOUR CASES OCCURRING IN A SINGLE GENERATION OF ONE FAMILY.

By N. E. Brill, A.M., M.D.,
ATTENDING PHYSICIAN TO THE MOUNT SINAI HOSPITAL,
F. S. Mandlebaum, M.D.,
PATHOLOGIST TO THE MOUNT SINAI HOSPITAL,
AND
E. Libman, M.D.,
ASSISTANT PATHOLOGIST TO THE MOUNT SINAI HOSPITAL, NEW YORK.

When our report of the pathological conditions found in one of the fatal cases of the family suffering from primary splenomegaly of the Gaucher type was published in March, 1905,[1] we were working at the organs of the sister of the patient who formed the subject of our report, and had promised to publish the pathological findings in this second case. After many delays we have finally succeeded in bringing our findings to publication.

The clinical histories of these two cases have been recorded.[2] The history of the second case may here be succinctly continued to the time of her death in September, 1904: Increasing anemia, increasing emaciation, increasing enlargement of the abdomen due to enormously increasing size of the spleen and liver were noted. Outside of a fracture of the third and fourth ribs on the right side, due to a fall in 1902, the patient was never confined to her house. These fractures healed without delay, with a large amount of callus. There were infrequent attacks of epistaxis, more frequent attacks of bleeding from the gums. Occasionally melena was noted, and on numerous occasions the feces gave positive reactions to the guaiac test. Ecchymoses occurred in the skin after the slightest injury. Pains referable to the ends of the femur and tibia were often complained of, but nowhere could bone tenderness be elicited. Sweating and hemorrhagic sudamina became more frequent. The brownish, uniform discoloration of the skin of the face and hands deepened. The hemoglobin gradually diminished to 35 per cent. (Dare instrument), although the red blood count at its lowest was 3,500,000. The white blood count still showed a tendency to leukopenia, the count being 3600 to 5200; no qualitative changes. There were no evidences of jaundice. Bile was absent from the blood serum and urine; the latter contained no urobilin.

Notwithstanding the apparently wretched appearance of the patient, which suggested a very serious illness, she showed an almost ceaseless activity, attending to domestic and social functions. She made no complaint of feeling ill outside of complaining of dyspnœa. On September 12, 1904, on crossing the street she was hit by a bicycle, which suddenly rounded the corner of the street, and knocked down, sustaining a fracture of the skull and laceration of the brain, from which she died that night.

---

[1] Primary Splenomegaly, Gaucher Type. Report on One of Four Cases Occurring in a Single Generation of One Family. Amer. Jour. Med. Sci., March, 1905.

[2] Amer. Jour. Med. Sci., April, 1901, and March, 1905.

Postmortem examination, September 13, 1904 (seven hours after death). Body length 155 cm. Marked emaciation; rigor mortis marked. Petechiæ in left conjunctiva, with large hemorrhages under the conjunctiva at the outer canthus. Hemorrhages are also present in the skin of the upper lids on both sides. No jaundice. Diaphragm on the right side at the second space; on the left side at the second rib. Cervical lymph nodes perceptible; axillary nodes not palpable; inguinal nodes perceptible. Small amount of clear, reddish fluid in the abdomen. Marked adhesion of the spleen to the abdominal wall and omentum. The spleen almost fills the entire abdominal cavity, extending about two fingers' breadth below the level of the superior spines of the ilium on both sides. The liver is adherent to the anterior abdominal wall. The small intestines lie below, behind, and to the right of the spleen. The stomach lies between the liver and the spleen, on the right side of the abdomen, the pylorus being situated posteriorly.

Over the occiput is a large hematoma, about 1.5 cm. thick and 7 cm. long. The brain is lacerated on the inner aspect of the frontal convolutions of the right side. Beneath the pia mater on the median surface of the right hemisphere is a large amount of blood. An extensive hemorhrage is also present over the entire external surface of the left hemisphere, and an extensive laceration of the left temporal lobe and third left frontal convolution is seen. The middle third of the median aspect of the right hemisphere is also lacerated. The line of fracture extends from the right posterior lacerated foramen across the transverse sinus to a point 2.5 cm. above and 2.5 cm. to the right of the torcular.

The heart weighs 215 grams. Fairly firm bands between visceral and parietal pericardium. Wall of right ventricle 0.5 cm. thick; left ventricle dilated, wall 1.25 cm. thick; right auricle dilated. Mitral valve slightly thickened, ring somewhat calcareous; aortic valve slightly insufficient (water test); some retraction of the flaps and thickening of their lines of attachment. Slight atheroma of aorta and coronaries. No congenital lesions. Heart muscle is brown in color. The lungs are non-adherent; fairly well expanded; anthracosis; moderate congestion. Bronchial nodes slightly enlarged and anthracotic. The spleen measures 45 x 25 x 13 cm.; and weighs 8.1 kilograms. There is recent and old perisplenitis. The pulp swells above the level of the cut surface. The color, as a whole, is salmon pink with grayish markings. There are no evidences of Malpighian bodies. Scattered throughout the spleen are large and small elevated areas which are firmer than the main bulk of the tissue. Most of these are red in color, with grayish and yellowish markings; a few are reddish at the margins and yellow at the centre. Besides these, a number of large, yellow, cheesy areas are seen, a few of which are very soft and are surrounded by a capsule. Splenic artery negative; splenic vein atheromatous. Near the hilum are a few small masses of accessory splenic tissue, pale yellowish in color. The liver is irregularly quadrate in form, very much enlarged; weight 3.9 kilograms. The width is 35 cm.; length of right lobe, 30 cm.; left lobe, 18 cm.; greatest thickness, 12 cm. Old and recent perihepatitis. The parenchyma swells above the cut section, is light browinsh in color, with irregular grayish markings. The outlines of the lobules are absent. On the under surface are a number of small hemorrhagic markings. The portal vein and the hepatic veins are negative. The gall-bladder is distended with dark, thick bile, containing a large number of very small, irregularly rounded stones, black in color. The wall of the gall-bladder appears to be normal; the ducts are pervious.

The kidneys combined weigh 270 grams. The right kidney measures 12 x 6 x 3.5 cm.; the left 13 x 7 x 3.5 cm. The left kidney is flattened, its capsule is adherent. The veins of the surface are injected, and a few dark depressions and small cysts are present. The cortex is swollen, and has a yellowish red color. On section the markings are poor; the medullary pyramids are intensely congested. The right kidney shows the same changes as the left, excepting that the medulla is less congested.

The right adrenal is large and flattened, and the medulla appears hemorrhagic. The left shows no changes. The stomach is much dilated; contains curdled milk. The ascending and transverse colon are moderately distended; the descending colon and sigmoid flexure are collapsed. The small intestine presents areas in which the vessels are very much distended and the mucosa swollen. The lymphoid follicles are very distinct and white in color, and especially prominent near the valve. The large intestine shows distention of veins and areas of inflammation, and lymphoid areas similar to those in the small intestine. The pancreas weighs 90 grams. The cut section shows congestion of the veins.

The mesenteric nodes are moderately enlarged; on section they are either entirely yellowish in color or dark red with yellowish markings. The retroperitoneal and iliac nodes, as well as the nodes of other parts of the abdomen, show the same changes as the mesenteric nodes. Some are the size of a pea, others as large as an almond. The iliac nodes are the size of an almond, and on section are either diffusely yellow in color or brownish black with yellow markings. The uterus is atrophic and virginal. There is an old hemorrhagic area in the right ovary, and remains of corpus luteum. The bladder shows injection of the vessels. The marrow of the vertebræ is normal. The cavity of the femur is filled with soft tissue which is dark red in color, with some yellowish areas.

Microscopic Findings. It may be stated at the outset that the lesions found in this case do not differ materially from those described in our first case, excepting that the changes in some of the organs are more advanced, as a result of the longer duration of the disease.

Spleen. The necrosis in this organ is very advanced. A study of the necrotic areas shows that the nuclei of the characteristic endothelial cells disappear somewhat earlier than the protoplasm. Large masses of endothelial cells are found, whose contours may still be recognized but whose nuclei are absent. Surrounding these necrotic areas are cells in which degenerative changes are apparent but in which the nuclei are regularly seen. A few capillaries are present in the necrotic areas, and small collections of pulp cells may be noted here and there. The hemorrhagic areas in this case are very extensive and are found in nearly all of the portions examined. More pigment is seen in this than in our previous case, and many of the cells are literally crowded with pigment granules. The distribution of the pigment is the same as in our earlier case, though here and there a few small particles are seen in the endothelial cells lining the capillaries. With these few exceptions, the sections present the same appearances that were described in full in our first case.

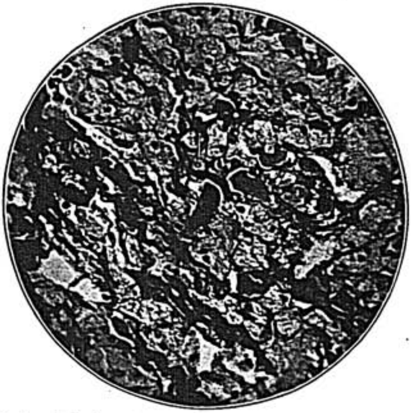

FIG. 1.—Section of the liver, showing endothelial cells in the meshes of the interlobular connective tissue. In the centre of the field are a few normal liver cells. (Photomicrograph × 250.)

Liver. The endothelial cells are very abundant in this organ and easily seen. As a rule, they are situated in the meshes of the interlobular connective tissue (Fig. 1), but a large number are also present in the lobule proper. In this situation they lie between the liver cells, without exerting any apparent pressure effects upon the latter (Fig. 2). With the low power the picture is that of a cirrhosis. A few of the characteristic endothelial cells are seen in the lumen of one large vein in the interlobular connective tissue. The pigment is the same as that described in our former case.

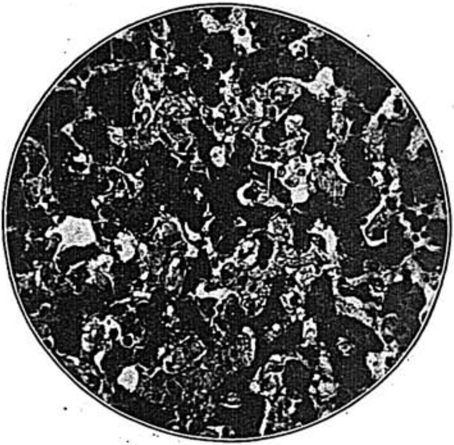

Fig. 2.—The centre of a liver lobule, showing a large number of endothelial cells lying between normal liver cells. (Photomicrograph × 250.)

Lymph Nodes. All of the nodes examined show the presence of a large number of endothelial cells, marked fibrous changes, and a great decrease or entire absence of adenoid tissue. The pigment is very abundant, confined, as a rule, to the sinuses bounded by the capsule and trabeculæ, and is crystalline in character for the most part. Chronic congestion is noted in all of the lymph nodes, but no hemorrhages are seen. Sections from the iliac nodes show by far the greatest amount of pigment as well as fibrosis, and almost complete absence of adenoid tissue. A careful study of the pigment in the iliac nodes shows that it is situated almost wholly in the endothelial cells throughout the entire node (Fig. 3). From one to four or five crystals are seen in each cell, the cytoplasm showing faintly between the adjacent crystals. Wherever the cytoplasm is invisible, the pigment crystals are still arranged in a more or less circular form, showing that they are contained in, and limited by, a spherical body (Fig. 4). In these nodes the endothelial cells are undoubtedly acting as phagocytes.

Bone Marrow. The endothelial cells are much more numerous than in our earlier case; in fact, some sections show hardly any remnants of normal marrow tissue. Other sections present a few islands of marrow cells here and there. The endothelial cells are compressed and distorted, as a rule, and a delicate connective-tissue reticulum is seen between them. A few large bloodvessels are present, also numerous capillaries. In one of the latter a distinct and typical endothelial cell is seen. The pigment is not abundant; when present, it is always situated in the immediate vicinity of the larger bloodvessels. The lesions in the other organs are not important, and have no bearing on the disease.

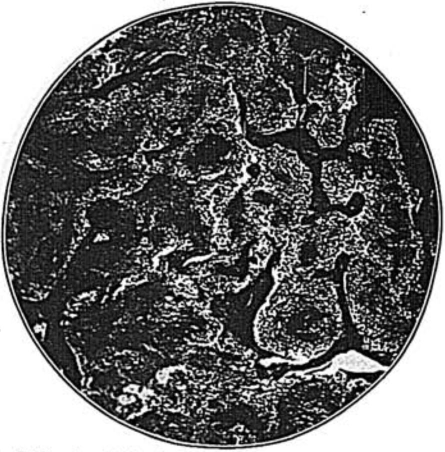

FIG. 3.—Section of an iliac lymph node, with complete absence of adenoid tissue. The entire section consists of connective-tissue reticulum and endothelial cells, the latter being filled with pigment crystals. (Photomicrograph × 45.)

REMARKS. Since the publication of our first case, in March, 1905, two more cases of splenomegaly of the Gaucher type have been recorded. One case was demonstrated by Schlagenhaufer[3] at a meeting of the German Pathological Society, September, 1906. The patient was a female, aged forty-one years, whose mother had suffered from tuberculosis thirty years ago. There were eight children, all of whom were healthy excepting one sister, who had an enlarged spleen. The patient had a "large abdomen" when five years of age, and at the age of twelve a large spleen was diagnosticated. Pigmentation of the face was noted nine years later. Examination of the blood showed hemoglobin, 65 per cent.; red cells, 4,700,000; leukocytes, 1300; the differential count was normal. Death was due to an acute cholangitis. Postmortem examination showed the following:

---

[3] Virch. Arch., 1907, clxxxvii, 125.

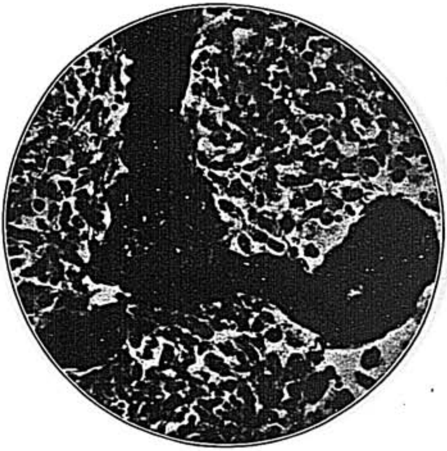

FIG. 4.—The same section shown in Fig. 3, showing the pigment crystals arranged in circular form or contained in endothelial cells. (Photomicrograph × 250.)

Skin of face and extremities yellow; face pigmented; icterus; right submaxillary glands enlarged and necrotic; no ascites. The spleen weighed 3510 grams, was of normal shape, reddish gray in color, and was studded with many nodules. The liver weighed 3000 grams. In the right lobe were multiple abscesses, in the left lobe several nodules. The mesenteric glands were large. The bone marrow was succulent in character and of a reddish color.

Microscopic examination of the spleen showed the usual picture found in the Gaucher type of splenomegaly. The pigment in certain situations, especially in the endothelial cells of the capillaries, did not give the iron reaction, while the pigment surrounding the blood-vessels gave the usual reaction. Tests for amyloid and fat were negative. Cultures showed the colon bacillus. Smears made from the necrotic parts showed tubercle bacilli, but these could not be demonstrated in sections. Guinea-pigs inoculated with necrotic portions showed tuberculosis. Sections from the lymph nodes showed the typical picture of splenomegaly; the submaxillary nodes contained tubercles. The right lobe of the liver was the seat of acute cholangitis with multiple abscesses; tubercles were found in both lobes. The bone marrow presented the usual picture found in these cases, together with the presence of tubercles.

Schlagenhaufer believes that splenomegaly is a systemic disease analogous to lymphosarcoma, excepting that the reticulum is involved and not the cellular structures. Furthermore, he doubts the endothelial origin of the characteristic cells, and considers that they arise from proliferated reticulum. He also believes that tuberculosis may have an important bearing on the etiology of the disease.

In the discussion that followed the presentation of this case, Schridde was of the opinion that the cells are endothelial in nature, and called attention to the fact that such cells are found normally in the spleen and lymph nodes, but not in the marrow.

Sternberg believed that in certain individuals these cells might be present normally in the bone marrow, and if so, would then proliferate in the presence of this disease. Two years before, he had described a proliferation of these cells in the lymphatic hemapoietic apparatus occurring in certain forms of tuberculosis, and had noted these cells in the bone marrow. Sternberg also criticised the parallel drawn by Schlagenhaufer between splenomegaly and lymphosarcoma: (1) Because splenomegaly is undoubtedly a congenital disease, which lymphosarcoma is not; and (2) because lymphosarcoma shows malignant characters, in direct contrast to the course of splenomegaly.

The second case was reported by Marchand[4] in March, 1907. The patient was a woman whose age is not mentioned. A splenic tumor had existed for twenty years, and the liver was also enlarged. A tendency to hemorrhage was present; the skin was icteric and had a brownish color; no leukocytosis. Banti's disease was diagnosticated. At the autopsy the spleen weighed 2720 grams; the color was grayish red; scattered nodules were present, some of which were necrotic; no follicles could be seen. The liver was also enlarged (weight not given), and whitish streaks were noted between the lobules. The lymph nodes in the abdomen were enlarged and pigmented. The bone marrow was pale reddish gray and contained grayish white spots. Microscopic examination revealed the characteristic cells in the spleen, liver, lymph nodes, and bone marrow.

---

[4] Münch. med. Woch., 1907, liv, 1102.

Marchand examined these organs in the fresh state and calls attention to the peculiar homogeneous, glassy, or hyaline appearance of the cells, similar to amyloid. Sections treated with osmic acid gave no reaction for fat. He does not look upon the process as a simple hyperplasia of the protoplasm, but believes that some foreign substance of unknown nature has been produced in the cells. This substance, when treated with the ordinary reagents employed in histological methods, reacts in a peculiar manner, and causes the streaked and wrinkled appearance of the cells noted, together with the formation of vacuoles and granules. According to Marchand, these cells may arise either from the reticulum or from endothelium.

From a study of our own cases, and a review of those published by others, we can state the following:

Splenomegaly (Gaucher type) is a distinct disease, starting in early life, often affecting several members of a family, and running a chronic course. It may be recognized by a great enlargement of the spleen, which precedes a similar enlargement of the liver, and is unaccompanied by jaundice or ascites; by the discoloration of the skin, especially where exposed to light; and by the absence in the blood of any characteristic findings. The disease has none of the characteristics of malignancy, and usually terminates as the result of an intercurrent affection. The organs affected are the spleen, liver, lymph nodes, and bone marrow. Histologically these organs show the presence of large cells with small nuclei and a peculiar hyaline cytoplasm, which arise from the endothelium or normal reticulum, and the presence of pigment containing iron. The etiology is unknown, though a peculiar susceptibility of the endothelium or reticulum of the hemapoietic apparatus to some unknown toxic agent is most likely present. There is nothing in our cases even suggesting tuberculosis. We would say that when found in cases of this disease, it must be considered as a superimposed process.

PRIMARY CARCINOMA OF THE LUNGS.

By A. L. Garbat, M.D.,
INTERNE AT THE GERMAN HOSPITAL, NEW YORK.

Primary carcinoma of the lungs, although not as rare as it is considered, and not as often diagnosticated as it might be, still warrants the reporting of every case that has been carefully studied both clinically and microscopically.

The author's patient was a male, aged sixty-four years, a German, and an insurance agent by occupation. Two of his brothers and one sister died of "galloping consumption," but no member of his